In the Claims

Please cancel claims 7, 21-31, 34, 36-39, 41, 45-62, 69-71, 73-78 and 82-87, without prejudice. Please amend claims 8-12, 32, 35, 40, 42, 63, 65, 79, 88, and add claims 101-109 as presented below in amended form:

In claims 8-12 and 93, please replace "7" with "101"

In claim 32, please replace "31" with "104".

In claim 42, please replace "26" with "41".

In claim 63, please replace "62" with "107".

In claim 79, please replace "78" with "108".

In claim 88, please replace "82" with "109".

35. (Amended) The method of claim 104 wherein R_1 is dimethoxytrityl, A has the formula -O-$(CH_2)_n$-NH- where n is 6, m is 2, R_4 is t-butoxy, R_5 is trifluoroacetoyl, R_6 is -C(=O)-$CH(CH_3)_2$, and R_{30} is FMOX.

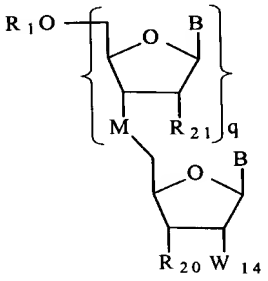
B4

40. (Amended) The method of claim 105 wherein R_1 is dimethoxytrityl, W_1 has the formula -O-$(CH_2)_n$-NH- where n is 6, m is 2, R_4 is t-butoxy, R_5 is trifluoroacetoyl, R_6 is -C(=O)-$CH(CH_3)_2$, and R_{30} is FMOX.

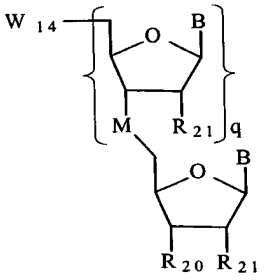
B5

B6 65. (Amended) The compound of claim 64 wherein R_4 is t-butoxy.

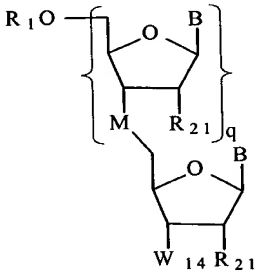
101. (New) A compound having formula XVIA, XVIB, XVIC or XVID:



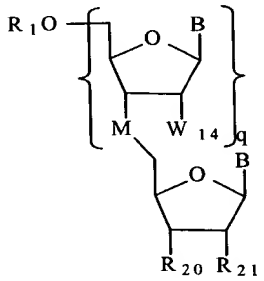
XVIA



XVIC



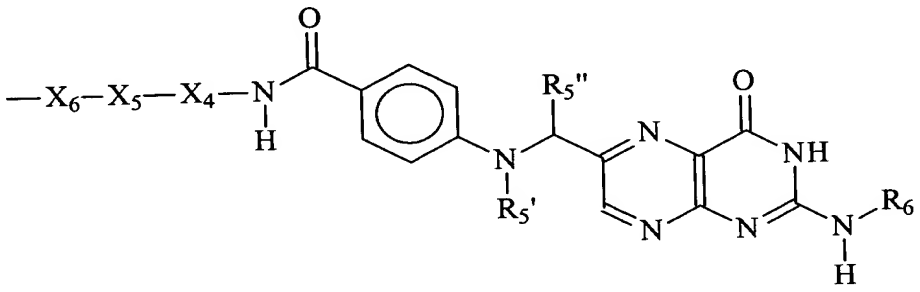
XVIB



XVID

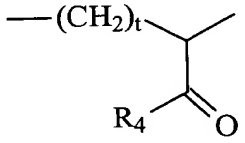
wherein:

W_{14} has the formula



wherein:

X_4 is -CH($X_{4'}$) or a group of formula:



$X_{4'}$ is the side chain of a naturally-occurring or non-naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid;

t is 1 or 2;

X_5 is -N($X_{6'}$)C(O)-, -C(O)NH-, -NHC(O)-, -OC(O)NH-,-C(S)NH-, -SC(S)NH-, -SC(O)NH-, -OC(S)NH-, -C(O)O-, -C(O)$(CH_2)_n$- or a bond;

n is an integer from 1 to 50;

each X_6 and $X_{6'}$ is, independently, a bond, hydrogen or a hydrocarbyl group selected from C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{20} alkynyl, C_6-C_{14} aryl, C_6-C_{14} aralkyl, C_3-C_{14} cycloalkyl, C_5-C_{14} fused cycloalkyl, C_4-C_{14} heterocycle, C_4-C_{14} heterocyclylalkyl, C_4-C_{14} heteroaryl and C_4-C_{14} heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups, and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; provided that X_6 is not hydrogen and $X_{6'}$ is not a bond;

R_1 is hydrogen or a hydroxyl protecting group;

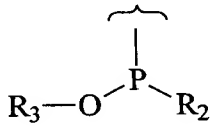
R_4 is a hydroxyl group or a protected hydroxyl group;

each $R_{5'}$ and R_{40} is, independently, hydrogen, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{20} alkynyl, C_6-C_{14} aryl or an amino-protecting group

$R_{5''}$ is hydrogen, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{20} alkynyl, C_6-C_{14} aryl, C_6-C_{14} aralkyl, C_3-C_{14} cycloalkyl, formyl, aminoalkyl or hydroxymethyl;

R_6 is hydrogen or an amino protecting group;

R_{20} is hydrogen or a group of formula:



R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms,

and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R_7 is straight or branched chain alkyl having from 1 to 10 carbons;

R_3 is a phosphorus protecting group;

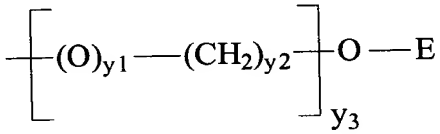
R_{21} is hydrogen, hydroxyl, fluoro or a group of formula $Z\text{-}R_{22}\text{-}(R_{23})_v$;

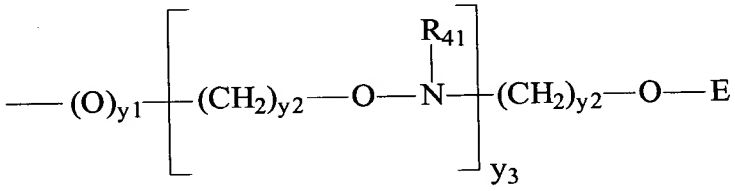
Z is O, S, NH or $N\text{-}R_{22}\text{-}(R_{23})_v$;

R_{22} is $C_1\text{-}C_{20}$ alkyl, $C_2\text{-}C_{20}$ alkenyl, or $C_2\text{-}C_{20}$ alkynyl;

R_{23} is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

or R_{21} has one of the formulas:





wherein:

y1 is 0 or 1;

each y2 is, independently, 0 to 10;

y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

B is a nucleobase;

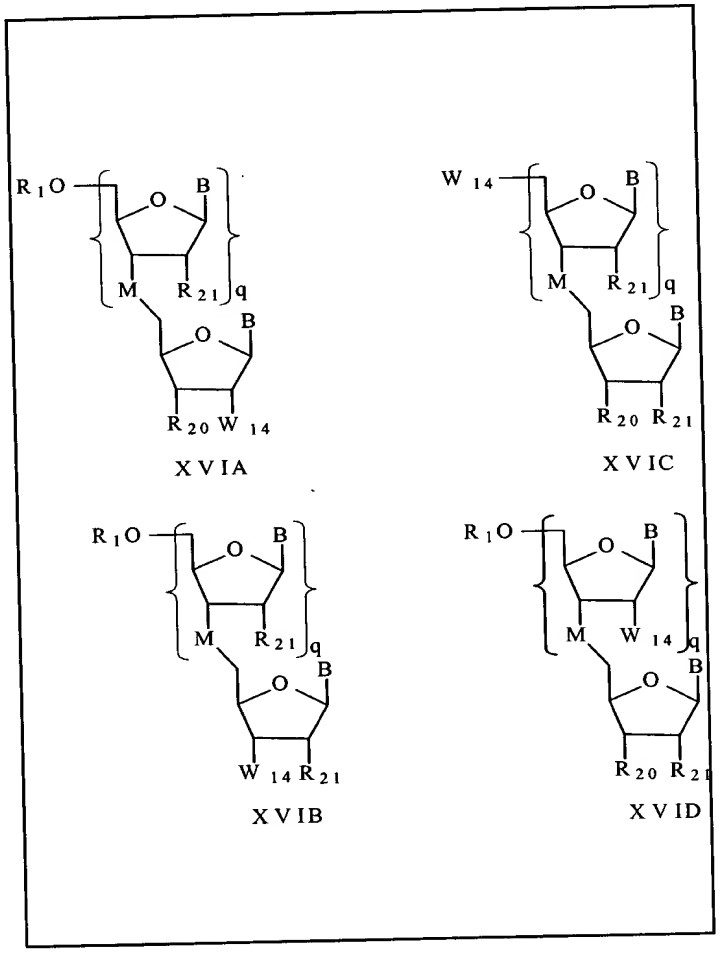
M is an optionally protected internucleoside linkage;

q is 0 to about 50; and

v is from zero to about 10;

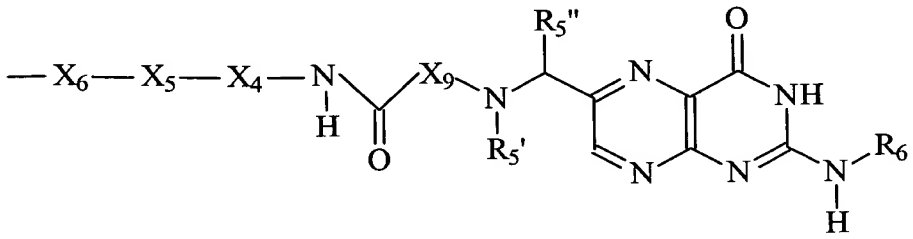
provided that when said compound has formula XVID, q is at least 1.

102. (New) A compound having formula XVIA, XVIB, XVIC or XVID:



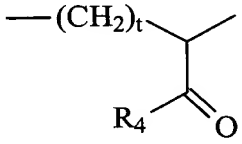
wherein:

W_{14} has the formula:



wherein:

X_4 is -CH($X_{4'}$) or a group of formula:



$X_{4'}$ is the side chain of a naturally-occurring or non-naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid;

t is 1 or 2;

X_5 is -N($X_{6'}$)C(O)-, -C(O)NH-, -NHC(O)-, -OC(O)NH-, -C(S)NH-, -SC(S)NH-, -SC(O)NH-, -OC(S)NH-, -C(O)O-, -C(O)$(CH_2)_n$- or a bond;

n is an integer from 1 to 50;

each X_6, $X_{6'}$ and X_9 is, independently, a bond, hydrogen or a hydrocarbyl group selected from C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{20} alkynyl, C_6-C_{14} aryl, C_6-C_{14} aralkyl, C_3-C_{14} cycloalkyl, C_5-C_{14} fused cycloalkyl, C_4-C_{14} heterocycle, C_4-C_{14} heterocyclylalkyl, C_4-C_{14} heteroaryl and C_4-C_{14} heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups, and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; provided that each X_6 and X_9 is not hydrogen and $X_{6'}$ is not a bond;

R_1 is hydrogen or a hydroxyl protecting group;

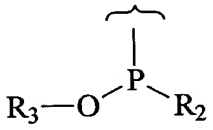
R_4 is a hydroxyl group or a protected hydroxyl group;

each $R_{5'}$ and R_{40} is, independently, hydrogen, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{20} alkynyl, C_6-C_{14} aryl or an amino-protecting group

$R_{5''}$ is hydrogen, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{20} alkynyl, C_6-C_{14} aryl, C_6-C_{14} aralkyl, C_3-C_{14} cycloalkyl, formyl, aminoalkyl or hydroxymethyl;

R_6 is hydrogen or an amino protecting group;

R_{20} is hydrogen or a group of formula:



R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R_7 is straight or branched chain alkyl having from 1 to 10 carbons;

R_3 is a phosphorus protecting group;

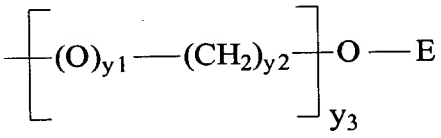
R_{21} is hydrogen, hydroxyl, fluoro or a group of formula $Z\text{-}R_{22}\text{-}(R_{23})_v$;

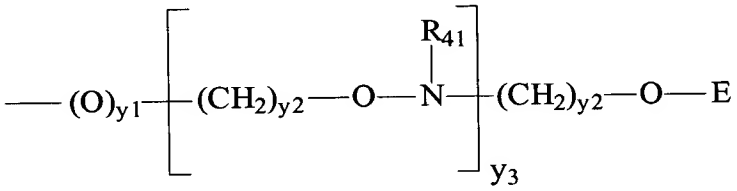
Z is O, S, NH or $N\text{-}R_{22}\text{-}(R_{23})_v$;

R_{22} is C_1-C_{20} alkyl, C_2-C_{20} alkenyl, or C_2-C_{20} alkynyl;

R_{23} is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

or R_{21} has one of the formulas:





wherein:

y1 is 0 or 1;

each y2 is, independently, 0 to 10;

y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N{=}C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom

selected from N and O;

B is a nucleobase;

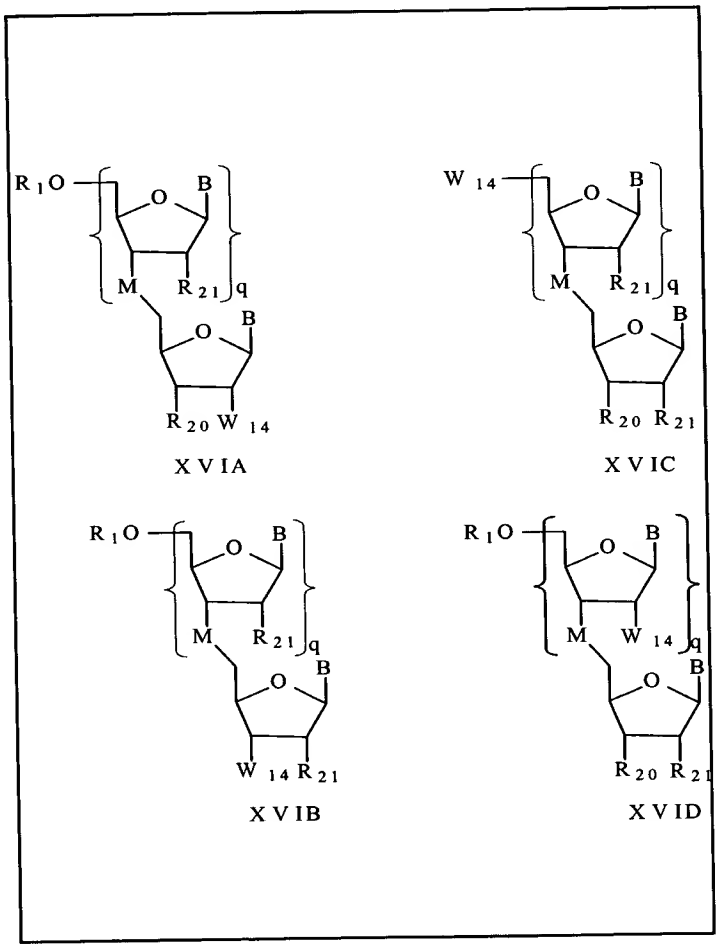
M is an optionally protected internucleoside linkage;

q is 0 to about 50; and

v is from zero to about 10;

provided that when said compound has formula XVIC, at least one R_{21} is a group other than hydrogen, and when said compound has formula XVIC or XVID, q is at least 1.

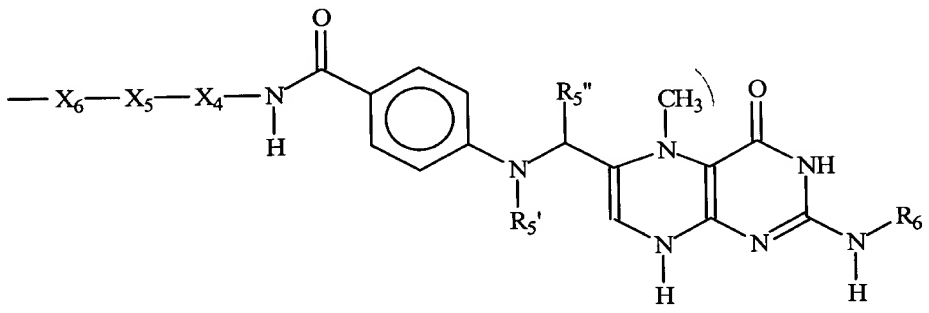
103. (New) A compound having formula XVIA, XVIB, XVIC or XVID:



XVIB XVID

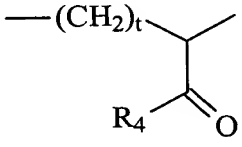
wherein:

W_{14} has the formula:



wherein:

X_4 is $-CH(X_{4'})$ or a group of formula:



$X_{4'}$ is the side chain of a naturally-occurring or non-naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid;

t is 1 or 2;

X_5 is -N($X_{6'}$)C(O)-, -C(O)NH-, -NHC(O)-, -OC(O)NH-, -C(S)NH-, -SC(S)NH-, -SC(O)NH-, -OC(S)NH-, -C(O)O-, -C(O)$(CH_2)_n$- or a bond;

n is an integer from 1 to 50;

each X_6 and $X_{6'}$ is, independently, a bond, hydrogen or a hydrocarbyl group selected from C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{20} alkynyl, C_6-C_{14} aryl, C_6-C_{14} aralkyl, C_3-C_{14} cycloalkyl, C_5-C_{14} fused cycloalkyl, C_4-C_{14} heterocycle, C_4-C_{14} heterocyclylalkyl, C_4-C_{14} heteroaryl and C_4-C_{14} heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups, and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; provided that X_6 is not hydrogen and $X_{6'}$ is not a bond;

R_1 is hydrogen or a hydroxyl protecting group;

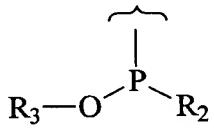
R_4 is a hydroxyl group or a protected hydroxyl group;

each $R_{5'}$ and R_{40} is, independently, hydrogen, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{20} alkynyl, C_6-C_{14} aryl or an amino-protecting group

$R_{5''}$ is hydrogen, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{20} alkynyl, C_6-C_{14} aryl, C_6-C_{14} aralkyl, C_3-C_{14} cycloalkyl, formyl, aminoalkyl or hydroxymethyl;

R_6 is hydrogen or an amino protecting group;

R_{20} is hydrogen or a group of formula:



R_2 is -N(R_7)$_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R_7 is straight or branched chain alkyl having from 1 to 10 carbons;

R_3 is a phosphorus protecting group;

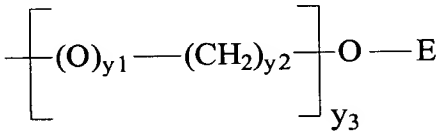
R_{21} is hydrogen, hydroxyl, fluoro or a group of formula $Z\text{-}R_{22}\text{-}(R_{23})_v$;

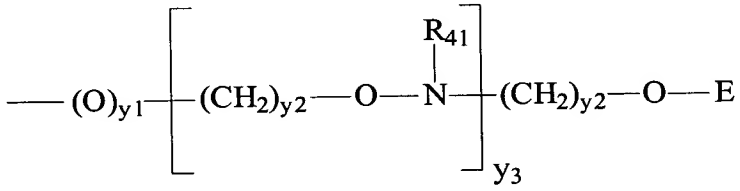
Z is O, S, NH or $N\text{-}R_{22}\text{-}(R_{23})_v$;

R_{22} is $C_1\text{-}C_{20}$ alkyl, $C_2\text{-}C_{20}$ alkenyl, or $C_2\text{-}C_{20}$ alkynyl;

R_{23} is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

or R_{21} has one of the formulas:





wherein:

y1 is 0 or 1;

each y2 is, independently, 0 to 10;

y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

B is a nucleobase;

M is an optionally protected internucleoside linkage;

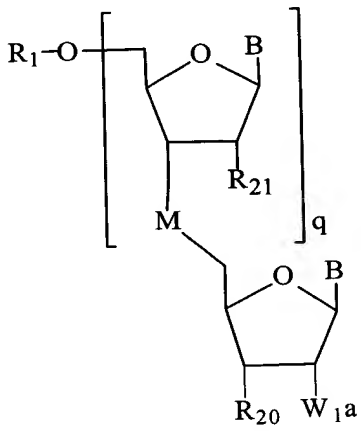
q is 0 to about 50; and

v is from zero to about 10;

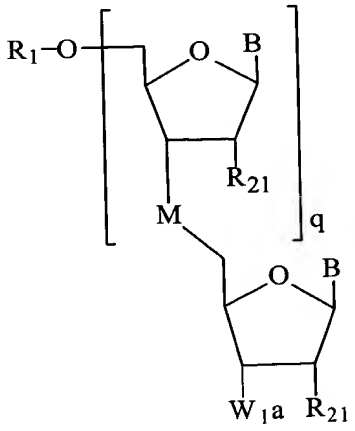
provided that when said compound has formula XVID, q is at least 1.

104. (New) A synthetic method comprising the steps of:

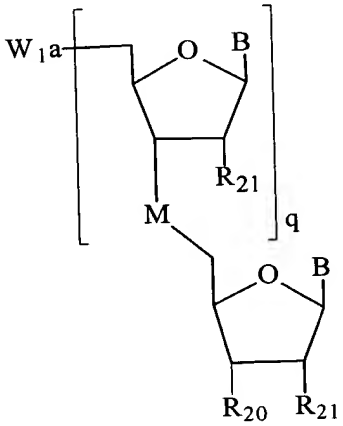
(a) providing a compound of formula IA, IB, IC or ID:



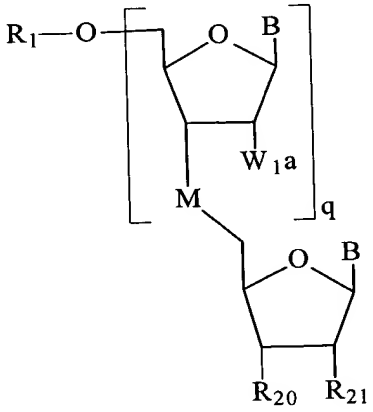
IA



IB



IC



ID

wherein:

W_{1a} is W_{1b}-H, OH, NH_2 or SH, where W_{1b} is a linking group;

R_1 is H or a hydroxyl protecting group;

B is a nucleobase;

each R_{21} is H, OH, F, or a group of formula $Z\text{-}R_{22}\text{-}(R_{23})_v$;

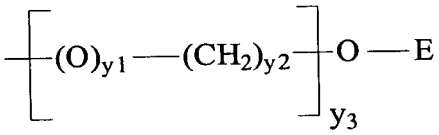
Z is O, S, NH, or $N\text{-}R_{22}\text{-}(R_{23})_v$

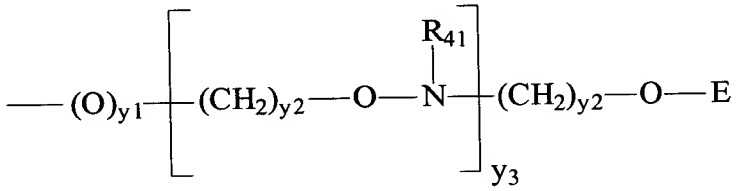
R_{22} is C_1-C_{20} alkyl, C_2-C_{20} alkenyl, or C_2-C_{20} alkynyl;

R_{23} is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

v is from 0 to about 10;

or R_{21} has one of the formulas:





wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

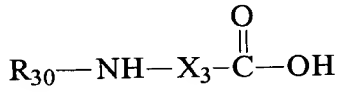
E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

q is from zero to about 50, provided that when said compound has formula ID, q is at least 1;

M is an optionally protected internucleoside linkage;

(b) reacting said compound of formula I with a compound of formula II:

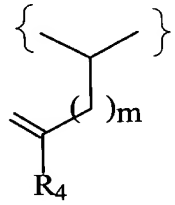


II

wherein:

R_{30} is an amino protecting group;

X_3 is a group of formula XII:

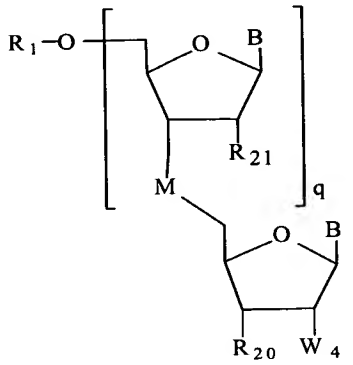


XII

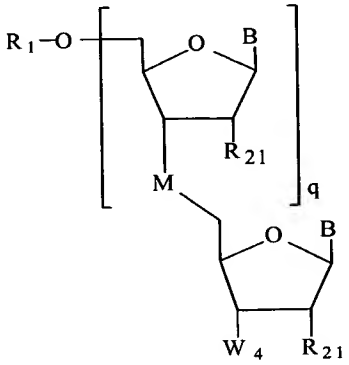
wherein m is 1 or 2;

R_4 is a hydroxyl group, or a protected hydroxyl group;

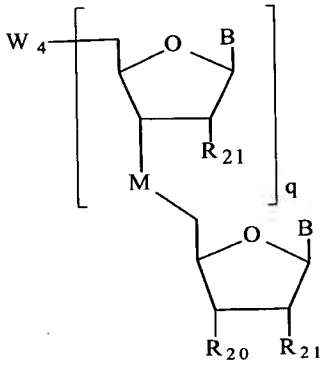
to form a compound of formula IVA, IVB, IVC, or IVD:



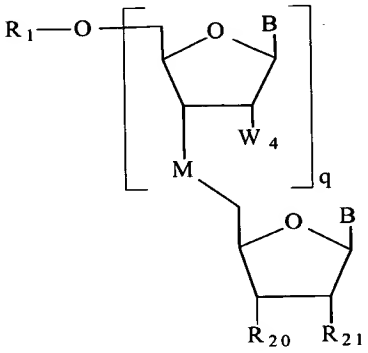
IVA



IVB



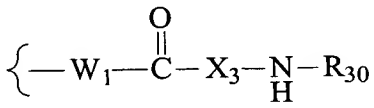
IVC



IVD

wherein:

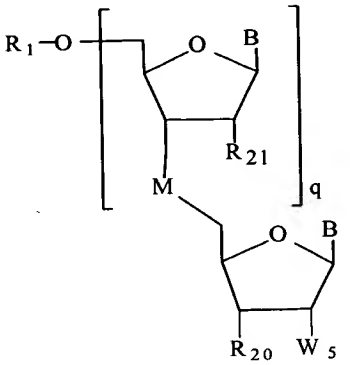
W_4 has the formula:



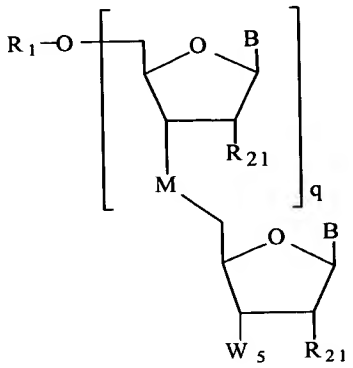
where W_1 is a linking group, O, NH, or S; and

treating said compound of formula IVA, IVB, IVC or IVD with a deprotecting reagent to form a

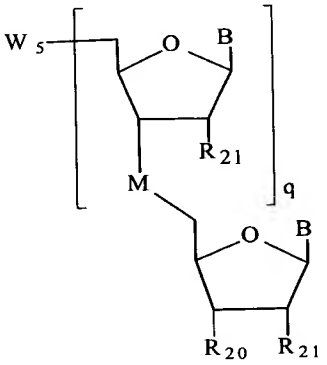
compound of formula VA, VB, VC or VD:



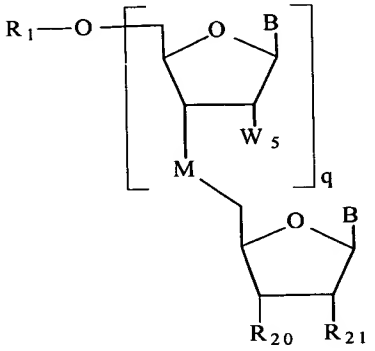
VA



VB

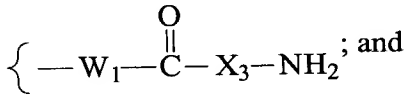


VC



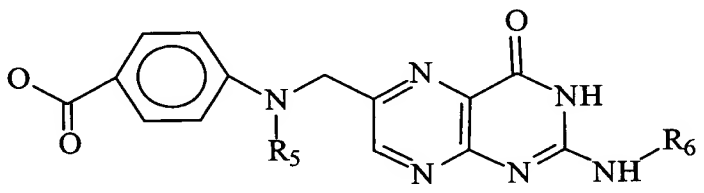
VD

wherein W_5 has the formula:



$$\left\{ -W_1-\overset{O}{\overset{\|}{C}}-X_3-NH_2 \right.$$; and

(c) condensing said compound of Formula V with a compound of Formula VI:



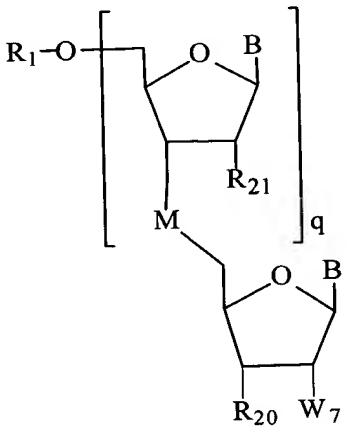
VI

wherein:

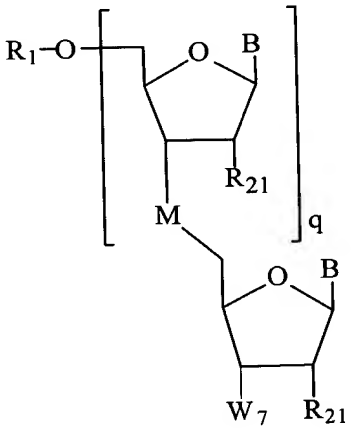
R_5 is H or an amino protecting group;

R_6 is H or an amino protecting group;

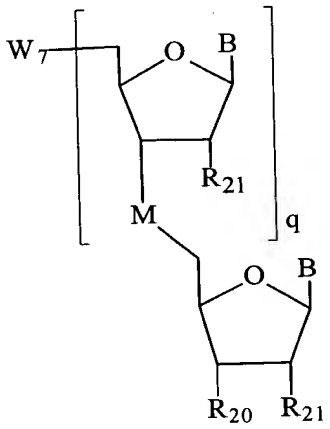
to form a compound of Formula VIIA, VIIB, VIIC, or VIID:



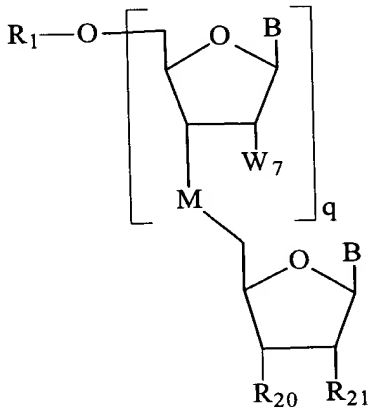
VIIA



VIIB

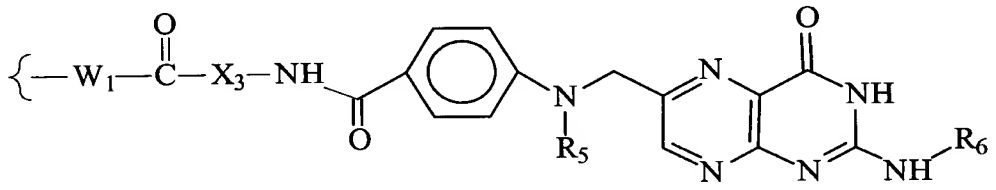


VIIC



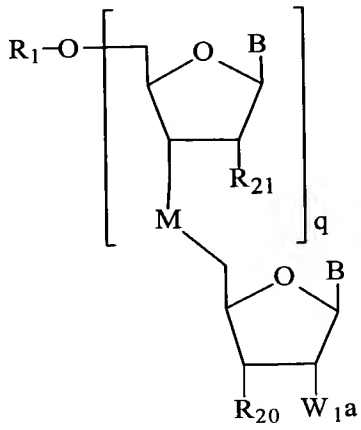
VIID

wherein W_7 has the Formula:

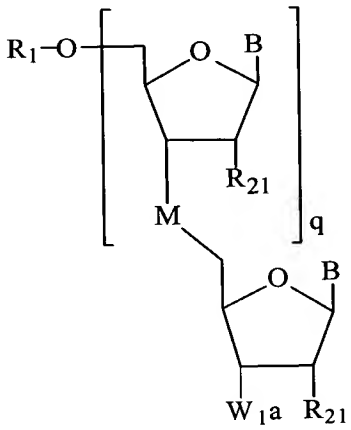


105. (New) A synthetic method comprising the steps of:

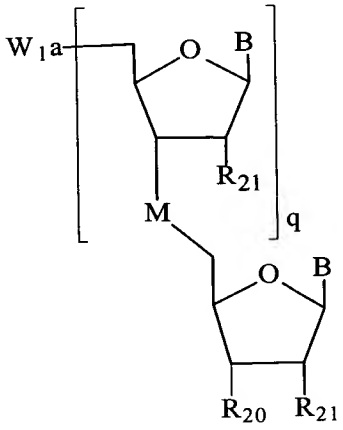
(a) providing a compound of formula IA, IB, IC or ID:



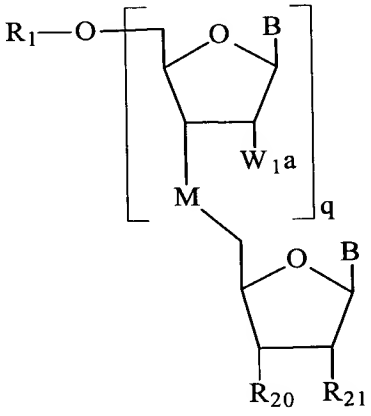
IA



IB



IC



ID

wherein:

W_{1a} is W_{1b}-H, OH, NH_2 or SH, where W_{1b} is a linking group;

R_1 is H or a hydroxyl protecting group;

B is a nucleobase;

each R_{21} is H, OH, F, or a group of formula $Z\text{-}R_{22}\text{-}(R_{23})_v$;

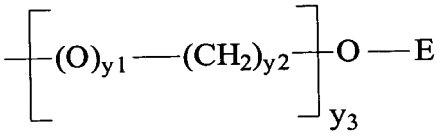
Z is O, S, NH, or $N\text{-}R_{22}\text{-}(R_{23})_v$

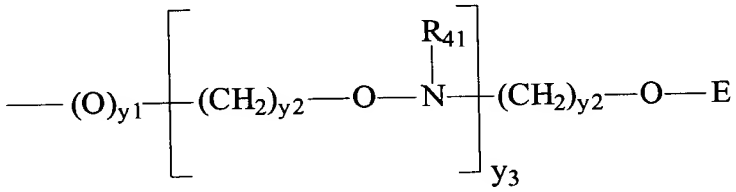
R_{22} is C_1-C_{20} alkyl, C_2-C_{20} alkenyl, or C_2-C_{20} alkynyl;

R_{23} is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

v is from 0 to about 10;

or R_{21} has one of the formulas:





wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

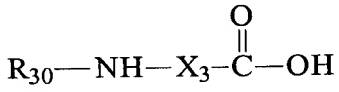
E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

q is from zero to about 50, provided that when said compound has formula ID, q is at least 1;

M is an optionally protected internucleoside linkage;

(b) reacting said compound of formula I with a compound of formula II:

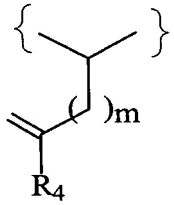


II

wherein:

R_{30} is an amino protecting group;

X_3 is a group of formula XII:

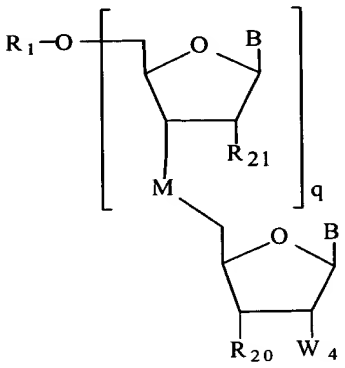


XII

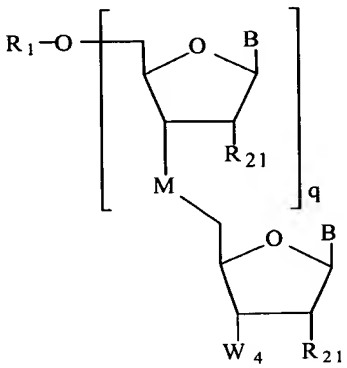
wherein m is 1 or 2;

R_4 is a hydroxyl group, or a protected hydroxyl group;

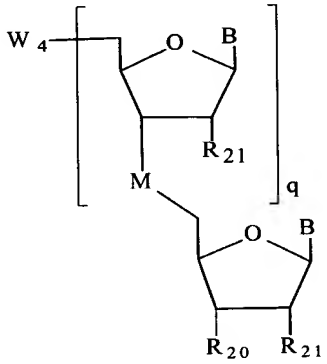
to form a compound of formula IVA, IVB, IVC, or IVD:



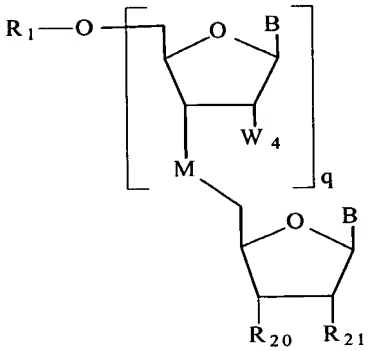
IVA



IVB



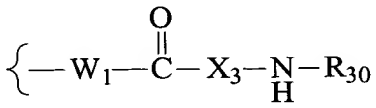
IVC



IVD

wherein:

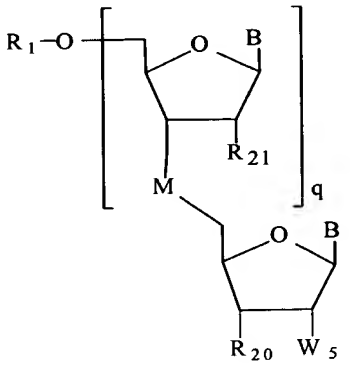
W_4 has the formula:



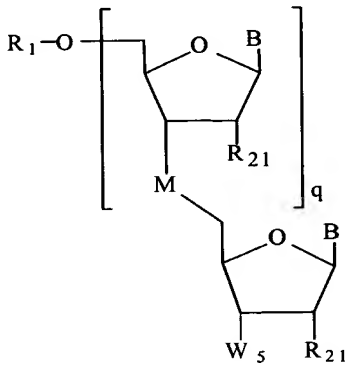
where W_1 is a linking group, O, NH, or S; and

treating said compound of formula IVA, IVB, IVC or IVD with a deprotecting reagent to form a

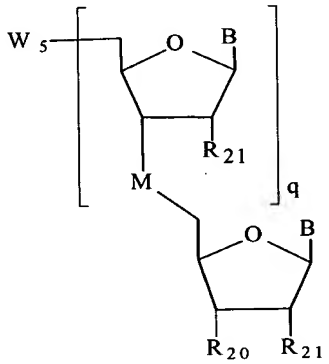
compound of formula VA, VB, VC or VD:



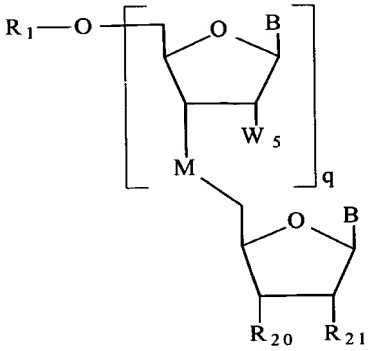
VA



VB



VC

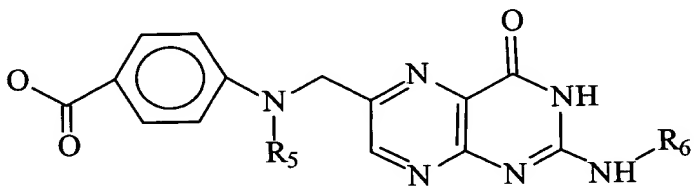


VD

wherein W_5 has the formula:

$$\left\{ -W_1-\overset{O}{\overset{\|}{C}}-X_3-NH_2 \right.; \text{ and}$$

(c) condensing said compound of Formula V with a compound of Formula VI:



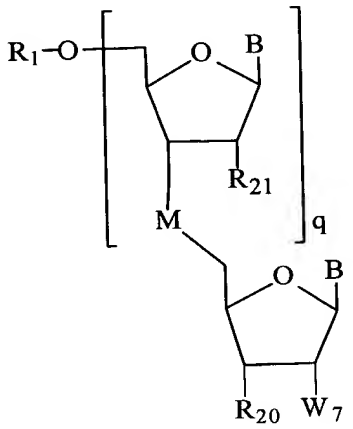
VI

wherein:

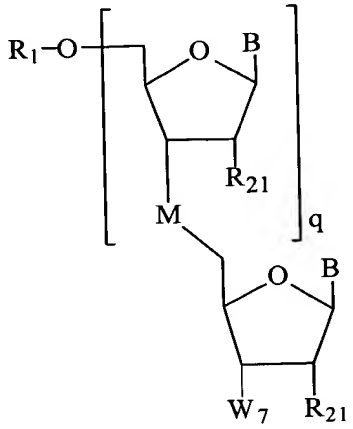
R_5 is H or an amino protecting group;

R_6 is H or an amino protecting group;

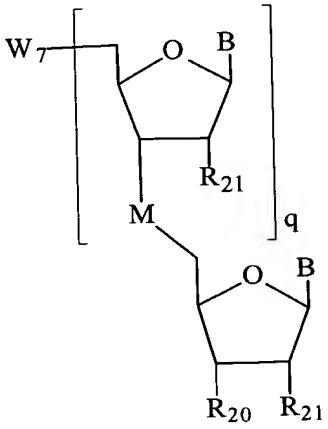
to form a compound of Formula VIIA, VIIB, VIIC, or VIID:



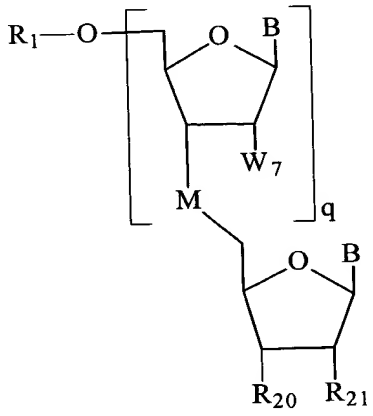
VIIA



VIIB

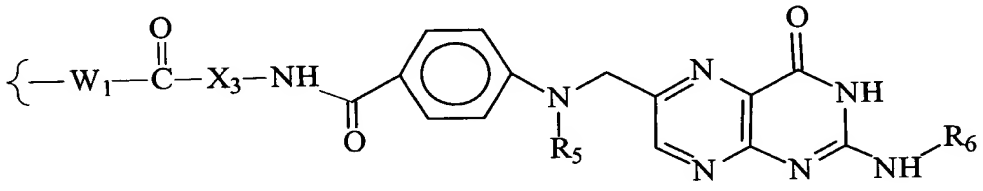


VIIC



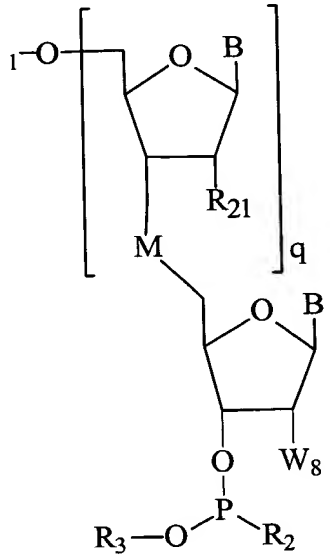
VIID

wherein W_7 has the Formula:

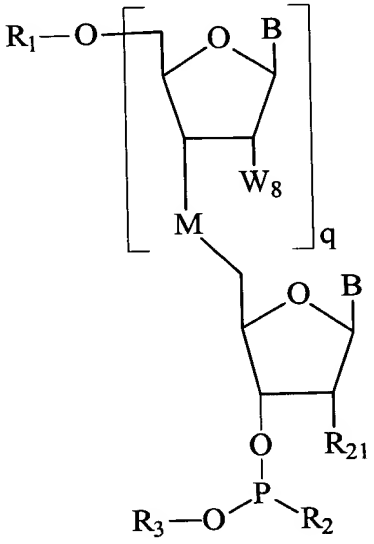


; and

(d) contacting said compound of Formula VIIA or VIID with a phosphitylating reagent to form a compound of Formula VIIIA or VIIID:

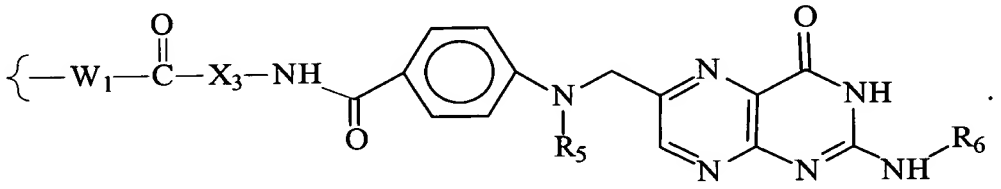


VIIIA



VIIID

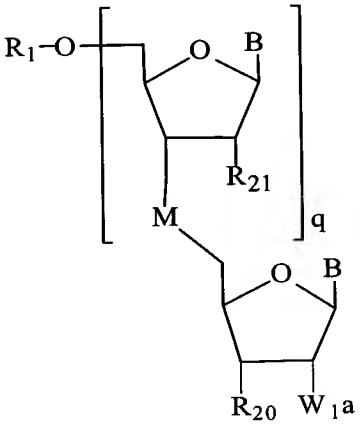
wherein W_7 has the Formula:



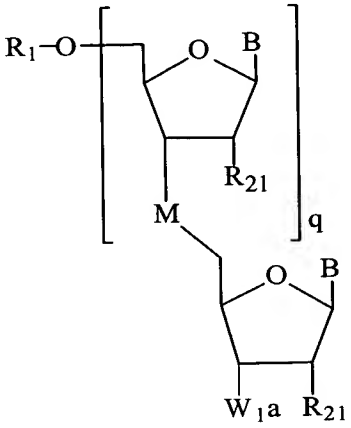
B7

106 (New). A synthetic method comprising the steps of:

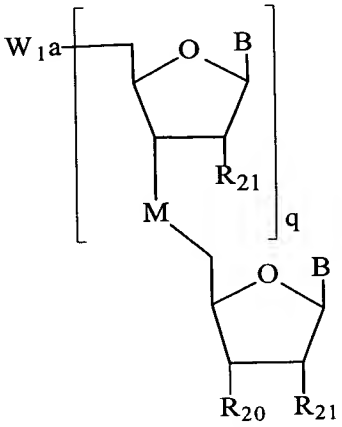
(a) providing a compound of formula IA, IB, IC or ID:



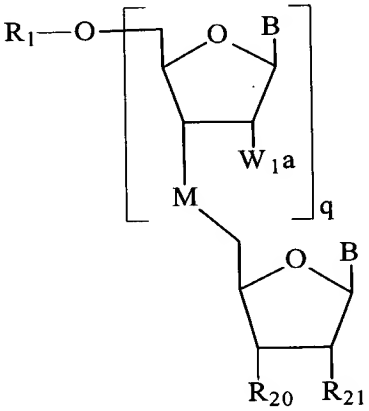
IA



IB



IC



ID

wherein:

W_{1a} is W_{1b}-H, OH, NH_2 or SH, where W_{1b} is a linking group;

R_1 is H or a hydroxyl protecting group;

B is a nucleobase;

each R_{21} is H, OH, F, or a group of formula $Z\text{-}R_{22}\text{-}(R_{23})_v$;

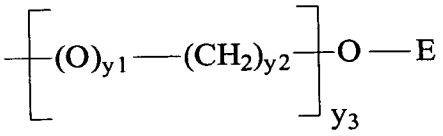
Z is O, S, NH, or $N\text{-}R_{22}\text{-}(R_{23})_v$

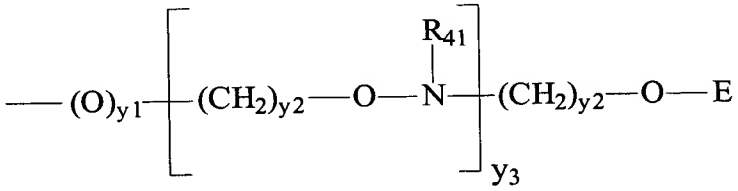
R_{22} is C_1-C_{20} alkyl, C_2-C_{20} alkenyl, or C_2-C_{20} alkynyl;

R_{23} is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

v is from 0 to about 10;

or R_{21} has one of the formulas:





wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

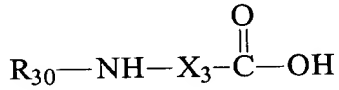
E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

q is from zero to about 50, provided that when said compound has formula ID, q is at least 1;

M is an optionally protected internucleoside linkage;

(b) reacting said compound of formula I with a compound of formula II:

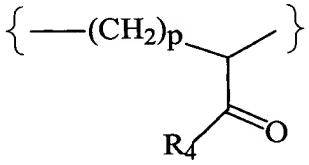


II

wherein:

R_{30} is an amino protecting group;

X_3 is a group of formula XI:



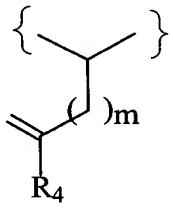
XI

wherein:

p is 1 or 2;

R_4 is a hydroxyl group, or a protected hydroxy group;

or X_3 is a group of formula XII:



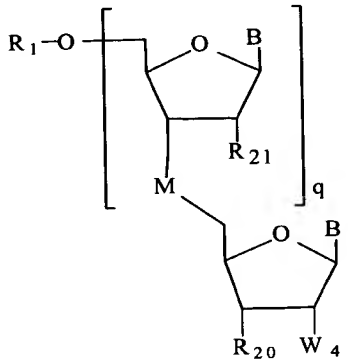
XII

wherein m is 1 or 2;

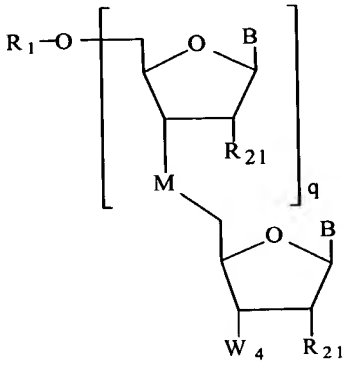
Z_1 is the sidechain of a naturally occurring amino acid, or a protected sidechain of a naturally occurring amino acid;

R_4 is a hydroxyl group, or a protected hydroxyl group;

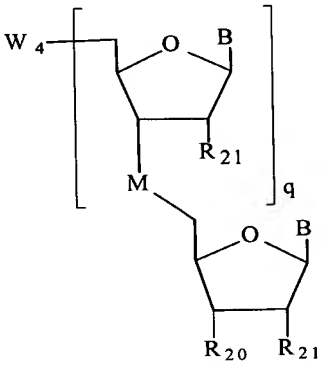
p is 1 or 2; to form a compound of formula IVA, IVB, IVC, or IVD:



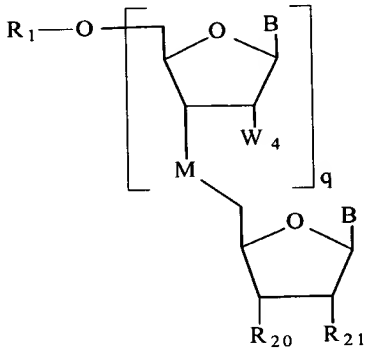
IV A



IV B



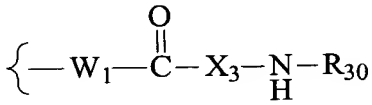
IV C



IV D

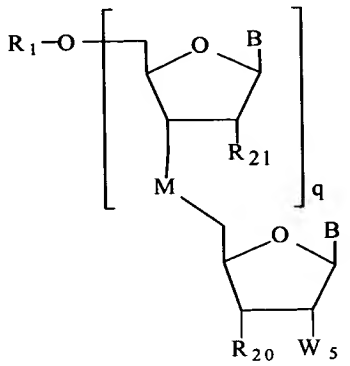
wherein:

W_4 has the formula:

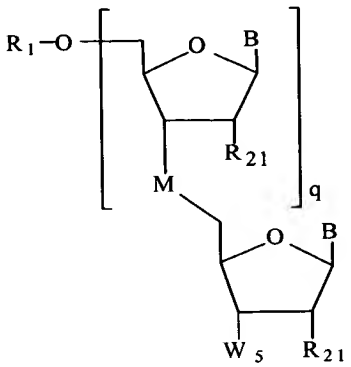


where W_1 is a linking group, O, NH, or S; and

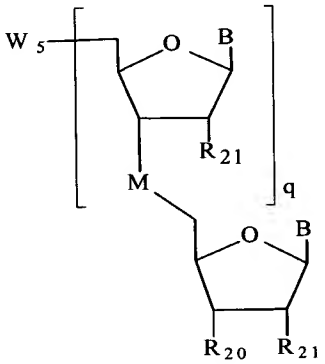
treating said compound of formula IVA, IVB, IVC or IVD with a deprotecting reagent to form a compound of formula VA, VB, VC or VD:



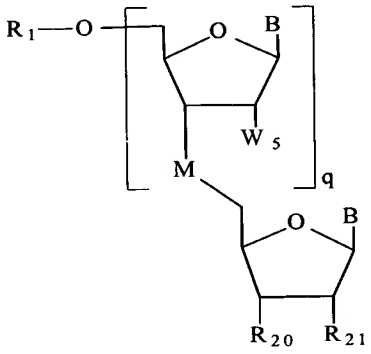
VA



VB



VC

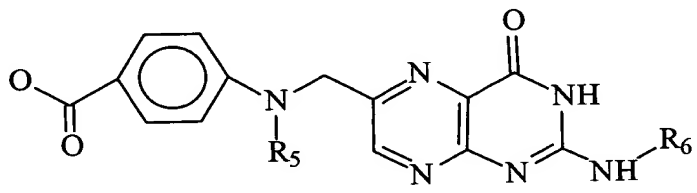


VD

wherein W_5 has the formula:

$$\left\{ -W_1-\overset{O}{\overset{\|}{C}}-X_3-NH_2 \right.; \text{ and}$$

(c) condensing said compound of Formula V with a compound of Formula VI:



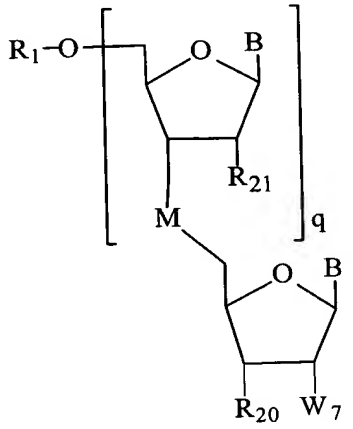
VI

wherein:

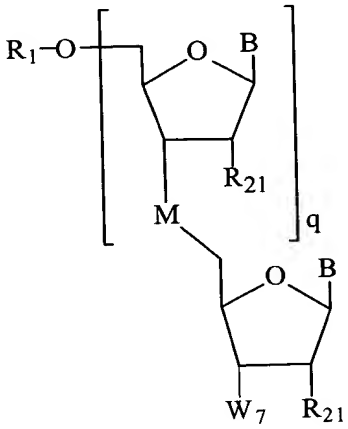
R_5 is H or an amino protecting group;

R_6 is H or an amino protecting group;

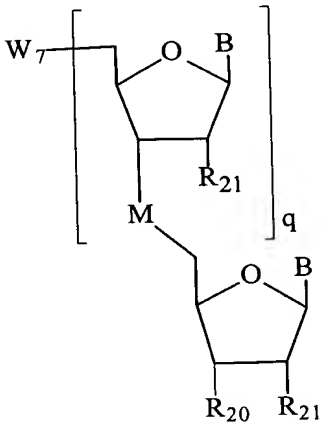
to form a compound of Formula VIIA, VIIB, VIIC, or VIID:



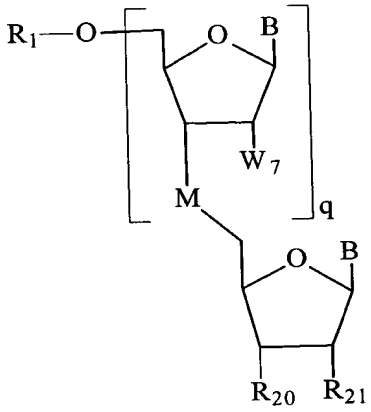
VIIA



VIIB

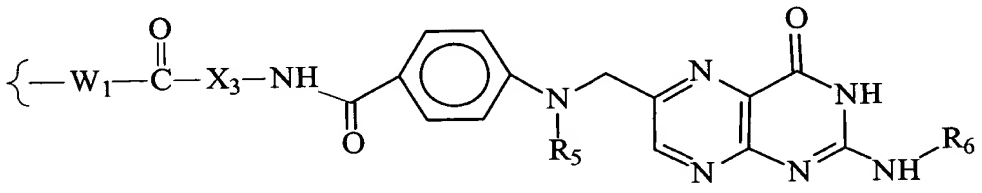


VIIC



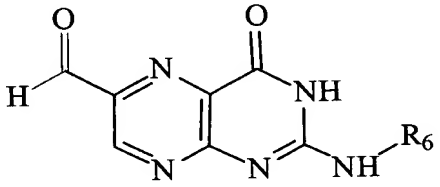
VIID

wherein W_7 has the Formula:



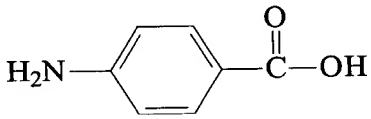
; and

wherein said compound of formula VI is prepared by the steps of reacting a compound of formula IX:



IX

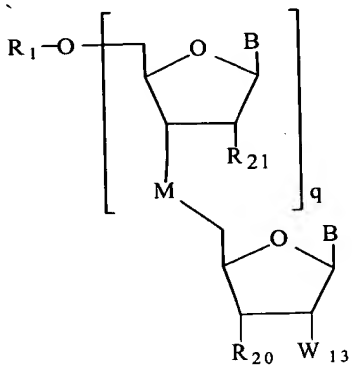
with a compound of formula X:



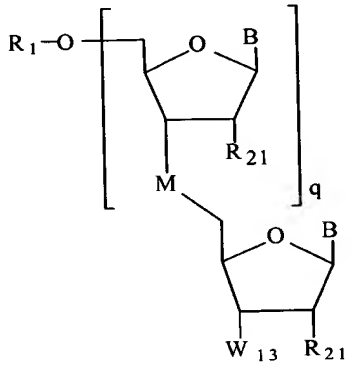
X

and treating the product of said reaction with a protecting group reagent to form said compound of formula VI.

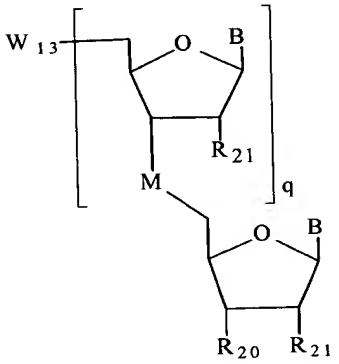
107. (New) A compound having the formula XIIIA, XIIIB, XIIIC or XIIID:



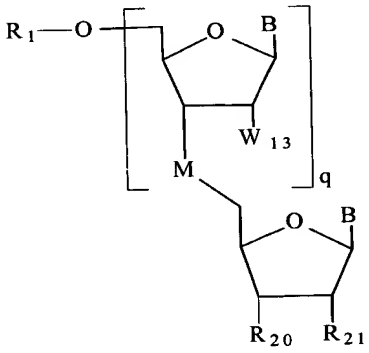
XIIIA



XIIIB



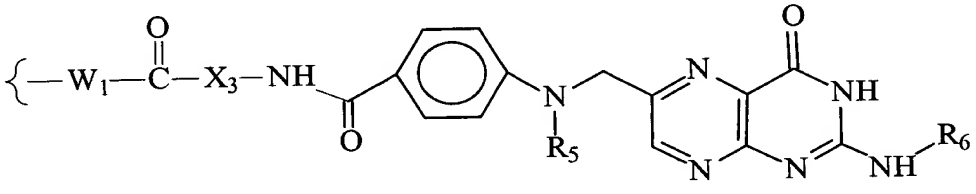
XIIIC



XIIID

wherein:

W_{13} has the formula:



R_1 is H or a hydroxyl protecting group;

B is a nucleobase;

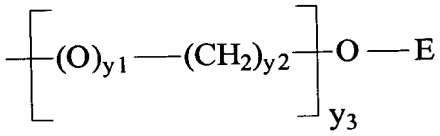
each R_{21} is H, OH, F, or a group of formula $Z\text{-}R_{22}\text{-}(R_{23})_v$;

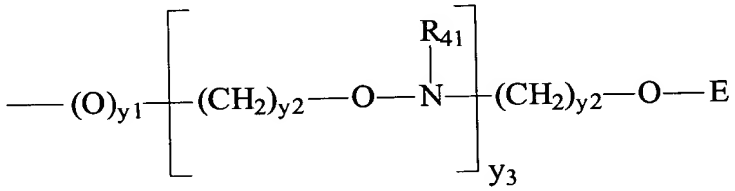
Z is O, S, NH or $N\text{-}R_{22}\text{-}(R_{23})_v$;

R_{22} is $C_1\text{-}C_{20}$ alkyl, $C_2\text{-}C_{20}$ alkenyl, or $C_2\text{-}C_{20}$ alkynyl;

R_{23} is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

or R_{21} has one of the formulas:





wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

v is from 0 to about 10;

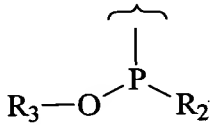
q is 0 to about 50; and

v is from zero to about 10;

M is an optionally protected internucleoside linkage;

W_1 is a linking group, O, NH or S;

R_{20} is H or a group of Formula:



R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

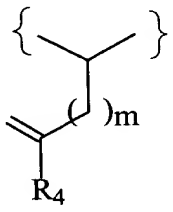
R_7 is straight or branched chain alkyl having from 1 to 10 carbons;

R_3 is a phosphorus protecting group;

R_5 is H or an amino protecting group;

R_6 is H or an amino protecting group;

X_3 has the formula XII:



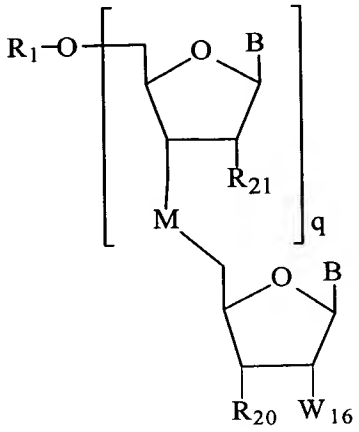
XII

wherein m is 1 or 2;and

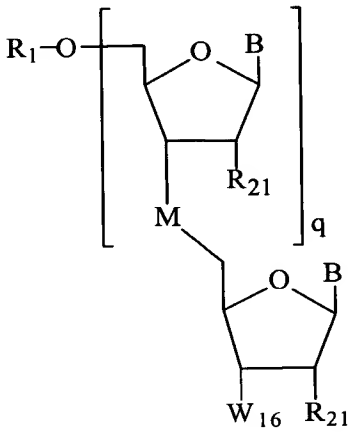
R_4 is a hydroxyl group, or a protected hydroxyl group;

provided that when said compound has formula XIIIC, at least one R_{21} is a group other than hydrogen, and when said compound has formula XIIIC or XIIID, q is at least 1.

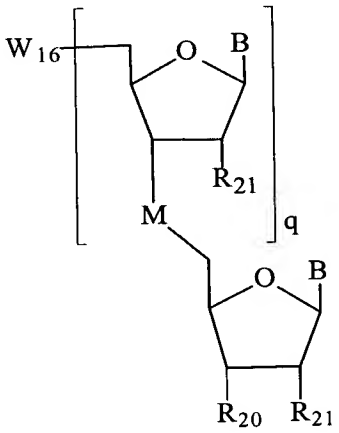
108 (New) A compound having the formula XVIA, XVIB, XVIC or XVID:



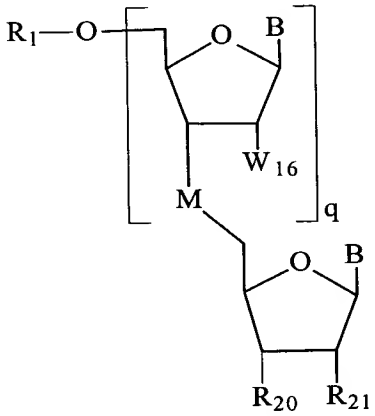
XVIA



XVIB



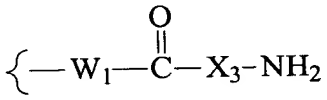
XVIC



XVID

wherein:

W_{16} has the formula:



R_1 is H or a hydroxyl protecting group;

B is a nucleobase;

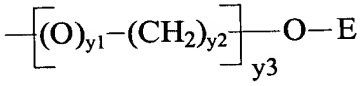
each R_{21} is H, OH, F, or a group of formula $Z\text{-}R_{22}\text{-}(R_{23})_v$;

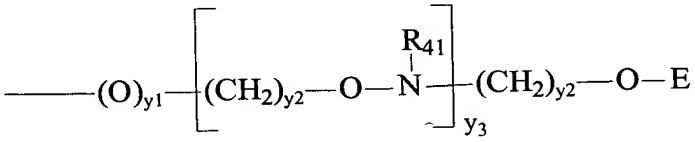
Z is O, S, NH or $N\text{-}R_{22}\text{-}(R_{23})_v$;

R_{22} is $C_1\text{-}C_{20}$ alkyl, $C_2\text{-}C_{20}$ alkenyl, $C_2\text{-}C_{20}$ alkynyl, $C_1\text{-}C_{20}$ akoxy, $C_2\text{-}C_{20}$ alkenyloxy, or $C_2\text{-}C_{20}$ alkynyloxy;

R_{23} is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

or R_{21} has one of the formulas:





wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

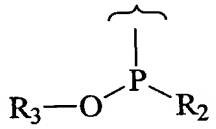
v is from 0 to about 10;

q is 0 to about 50;

M is an optionally protected internucleoside linkage;

W_1 is a linking group;

R_{20} is H or a group of Formula:

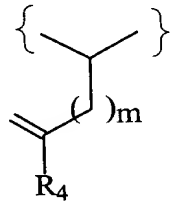


R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R_7 is straight or branched chain alkyl having from 1 to 10 carbons;

R_3 is a phosphorus protecting group;

X_3 has the formula XII:



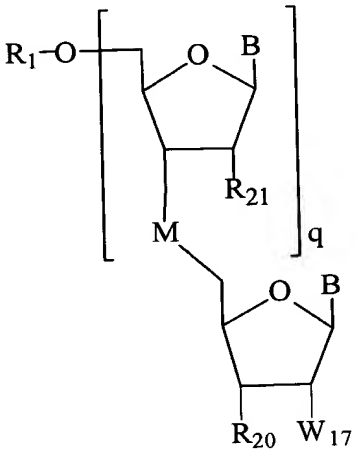
XII

wherein m is 1 or 2;

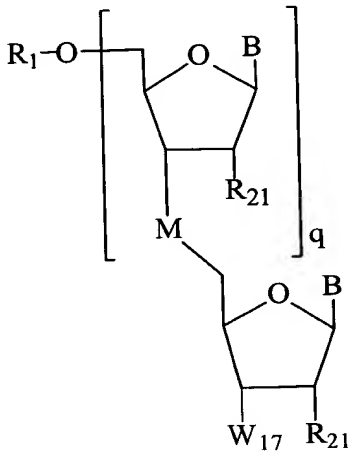
R_4 is a hydroxyl group, or a protected hydroxyl group; and

provided that when said compound has formula XVID, q is at least 1.

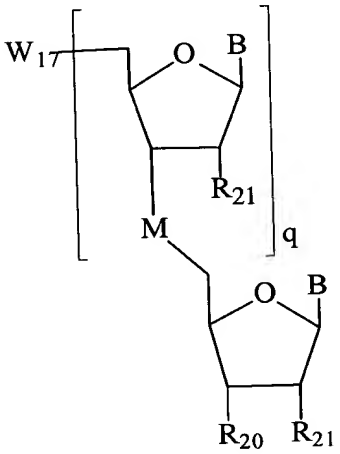
109. (New) A compound having the formula XVIIA, XVIIB, XVIIC or XVIID:



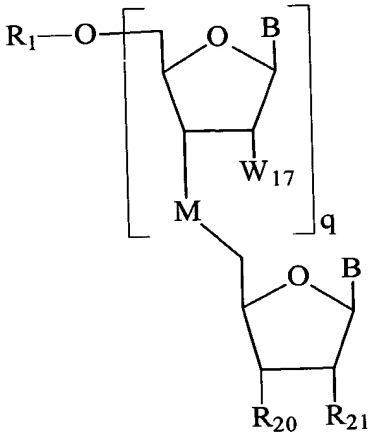
XVIIA



XVIIB



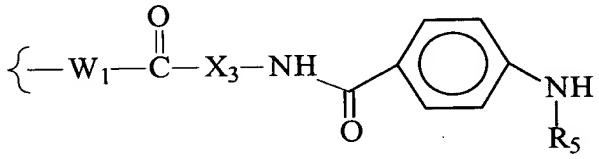
XVIIC



XVIID

wherein:

W_{17} has the formula:



R_1 is H or a hydroxyl protecting group;

B is a nucleobase;

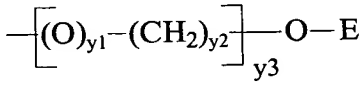
each R_{21} is H, OH, F, or a group of formula $Z\text{-}R_{22}\text{-}(R_{23})_v$;

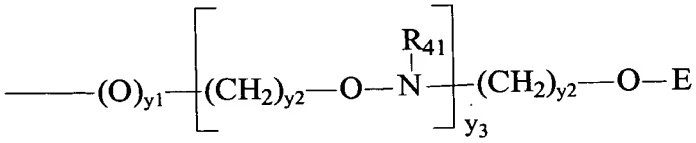
Z is O, S, NH or $N\text{-}R_{22}\text{-}(R_{23})_v$;

R_{22} is $C_1\text{-}C_{20}$ alkyl, $C_2\text{-}C_{20}$ alkenyl, or $C_2\text{-}C_{20}$ alkynyl;

R_{23} is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

or R_{21} has one of the formulas:





wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

E is $N(R_{41})(R_{42})$ or $N=C(R_{41})(R_{42})$;

each R_{41} and each R_{42} is independently H, C_1-C_{10} alkyl, a nitrogen protecting group, or R_{41} and R_{42} taken together form a nitrogen protecting group; or R_{41} and R_{42} taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

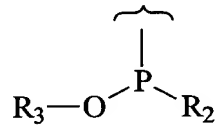
v is from 0 to about 10;

q is 0 to about 50;

M is an optionally protected internucleoside linkage;

W_1 is a linking group, O, NH or S;

R_{20} is H or a group of Formula:

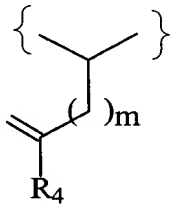


R_2 is $-N(R_7)_2$, or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R_7 is straight or branched chain alkyl having from 1 to 10 carbons;

R_3 is a phosphorus protecting group;

X_3 has the formula XII:



XII